## REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

### I. CLAIM STATUS AND AMENDMENTS

Claims 1-5, 7, 11, 13-17 and 19 were pending in this application when last examined.

Claims 1-5 and 7 were examined on the merits and stand rejected.

Claims 11, 13-17 and 19 were withdrawn as non-elected subject matter. Applicants reserve the right to file a Continuation or Divisional Application on any withdrawn subject matter.

Claims 1-5, 7, 11, 13-17 and 19 are pending. Claims 1-5 and 7 are under examination and are currently rejected.

### II. OBVIOUSNESS REJECTION

On pages 2-5 of the Office Action, claims 1-5 were rejected under 35 U.S.C. 103(a) as obvious over Chenchik et al. in view of Brennan et al. Further, on pages 7-9, claims 1-5 and 7 were rejected under 35 U.S.C. 103(a) as obvious over Okayama et al. in view of Brennan et al.

Applicants respectfully traverse this rejection.

Initially, it is noted that the claimed invention requires that the 3' end of the first strand cDNA is ligated to the 5' end of the first strand of the double-stranded DNA primer using T4 RNA ligase. Referring to figure 1 of the specification, it is therefore apparent that T4 RNA ligase ligates together a cDNA/mRNA heteroduplex to a double-stranded DNA.

Brennan et al. describes that a short DNA oligomer can be circularized and joined intermoleculary. However, the short DNA of Brennan is a single-stranded DNA.

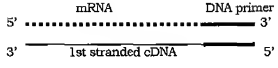
The Examiner of the position that the art supports that DNA oligomer can be ligated to DNA using T4 RNA ligase in intramolecular reactions as suggested by Brennan et al.

In particular, the Examiner refers to a second paragraph of page 39 of Brennan et al. However, the Examiner is directed to the second sentence of this paragraph:

> *We have found conditions under which 2'-deoxyribonucleoside 3',5'-biophosphates can be added to DNA oligomers and single-stranded DNA oligomers be joined in good yields.*[15-18]

Such sentence therefore indicates that single stranded DNA oligimers can be joined in good yield. Such is not a teaching of joining a double-stranded DNA to a cDNA/mRNA heteroduplex as required in the claimed invention.

In the present invention, the mRNA/cDNA heteroduplex is circularized using T4 RNA ligase. The heteroduplets is as follows:




The heteroduplex is circularized by ligating the 3' end of the first strand cDNA to the 5' end of the first strand of the double-stranded DNA primer using T4 RNA ligase. However, this is not equivalent to circularization of a single-stranded DNA using T4 RNA ligase. Please note that the heteroduplex is a double-stranded form, and further **one end** of the heteroduplex is **double-stranded DNA.**

It is known that DNA ligase is used for circularization of double-stranded DNA, and RNA ligase is for circularization of single-stranded DNA or RNA. However, there is no cited art regarding circularization of an RNA/DNA heteroduplex. The present invention was completed by a finding that the heteroduplex can be circularized by T4 RNA ligase. This is not due to the teachings of Brennan nor any other common knowledge.

None of the other references cited by the Examiner remedy this deficiency in Brennan. Thus, these obviousness rejections are untenable and should be withdrawn.

## CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

Seishi KATO et al.

/William R. Schmidt, II/

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January 31, 2011